

EUROPEAN TERATOLOGY SOCIETY
20TH ANNUAL CONFERENCE
31 AUGUST - 3 SEPTEMBER 1992

CONGRESS CENTRE/HOTEL MARITIM
WÜRZBURG, GERMANY

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were musculoskeletal (27%) and cardiovascular (18%). Among the 244 multimalformed babies, a chromosomal anomaly was found in 54 cases (22%), a monogenic inheritance in 17 (7%), a recognized condition in 59 (24%). In this latter group there were 36 cases of Robin sequence. A significant predominance of males was found among CLP ($P < .01$, sex ratio 283/174) and of females among CP ($P < .05$ sex ratio 140/168). Of several environmental factors considered, only epilepsy is consistently related to isolated clefts ($P < .01$). Consistent with a more important role of hereditary factors in isolated CLP, a significant association with consanguinity ($P < .01$) and with the presence of congenital anomalies in the family ($P < .01$) were found.

P7

CANAVESE B., COLITTI M. and COLLETTA I., Department of Animal Production Sciences, University of Udine, Italy. Blood cells forms and quantitative values in normal and NTD chick embryos at the end of incubation

The chick embryos with spontaneous neural tube defects (NTD) were collected still alive on the 21st day of incubation (Canavese, 1979) and classified as exencephalic and anencephalic merocranial (Lemire et al., 1978; Colitti and Canavese, 1989). Before drawing blood by heart injection, the embryos were anaesthetized with ether; samples of blood, collected in EDTA, were prepared for observations under LM and SEM and for haematological determinations (Hb, PCV, MCV, MCH, MCHC). Also normal and with congenital cerebral hernia (Polish) embryos, at the same age of the NTD, were examined. Count of RBC, PCV and Hb values were significantly lower in the NTD embryos, whereas the differential counts of leucocyte were not. Moreover, various irregular forms of blood cells in the serious NTD embryos were observed (poikilocytosis, "tear drops" forms, etc.). The authors stressed consequences that NTD defects have on the haematological profile and importance of further investigations.

P8

DRUGA, Alice and DENCKER, L., Institute for Drug Research, Budapest, Hungary, and Dept. of Toxicology, Uppsala University, Uppsala, Sweden. Mode of action studies with perphenazine on chondrocyte differentiation in vitro.

Perphenazine (PPZ) induced skeletal malformations in rats and the histological examination of bone anlage

revealed the disturbance of enchondral ossification process. An expressed accumulation of labelled PPZ was detectable by autoradiography in the skeletons. As an effect on prechondrocytes was presumed the *in vitro* spot culture of prechondrogenic chick embryo limb buds was chosen for the mode of action studies. 2.5, 5, 10, and 20 μM concentrations were applied for various culture periods and the development of cultures, as well as the incorporation of labelled thymidine and sulfate were measured by liquid scintillation. Both the thymidine and sulfate incorporations were primarily inhibited by PPZ during the first 2 to 4 days of treatment showing also a concentration dependency, while the late addition of PPZ did not influence significantly these values. The results demonstrated delayed differentiation of mesenchymal cells and impaired function of the prechondrocytes and chondrocytes.

The *in vitro* studies were supported by the grants of Uppsala University and European Science Foundation (1986 and 1991).

P9

GALÓGZY, K., A. POTOCZKI, E.G. KARSAI, M. SÖNFELD, M.M. LENGYEL, Chemical works of Gedeon Richter Ltd, Pharmacological Research Centre, Department of Reproduction Toxicology, Budapest, Hungary. Peri-postnatal study of Pyladox^R in the RG-HW rat

We made the peri-postnatal study of TRH-analogue Pyladox with the doses applied in DAINIPPON Pharmaceutical Co. at doses levels of 1, 10 and 100 mg/kg. Test compound was administered from gestation day 15 till postnatal day 21 once daily intravenously to pregnant and delivered rats to evaluate the effect of Pyladox on the process of birth, the offsprings, the lactation and the offsprings' care. Altogether 56 dams and 524 offsprings were evaluated. Females were examined for survival, clinical symptoms, food consumption, body weight change, reproductive parameters, organ weight and autopsy findings. Offspring were evaluated for viability, body weight, organ weight, and autopsy findings. Offsprings' examinations for somatic development were: body weight, ears raised, teeth eruption, eyes opening. Reflex development examinations were: righting reflex, response to pain, traction test and cornea reflex. Drug related alterations were not found in examined parameters in the females, alterations not observed in somatic and reflex development of pups.

